SEQUENCE LISTING

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<110> Hall, Barry G.
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<120> METHOD OF DETERMINING EVOLUTIONARY POTENTIAL OF MUTANT RESISTANCE GENES AND USE THEREOF TO SCREEN FOR DRUG EFFICACY

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<150> 60/149,813

<151> 1999-08-19

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<170> PatentIn Ver. 2.1

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<210> 4
<211> 1134
<212> DNA
<213> Unknown Organism
<220>
<223> Description of Unknown Organism: Escherichia coli plasmid pBR322
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<400> 4 atggtcaaaa cgacgctctg cgccttatta attaccgcct cttgctccac atttgctgcc 60 cctcaacaaa tcaacgatat tgtgcatcgc acaattaccc cgcttataga gcaacaaaag 120 atcccgggta tggcggtggc ggtaatttat cagggtaaac cttattactt tacctggggc 180 tatgcggaca tcgccaaaaa gcagcccgtc acacagcaaa cgttgtttga gttaggttcg 240 gtcagcaaaa catttactgg cgtgcttggt ggcgacgcta ttgctcgagg ggaaatcaag 300 ttaagcgatc ccacaacaaa atactggcct gaacttaccg ctaaacagtg gaatgggatc 360 acactattac atctcgcaac ctacactgct ggcggcctgc cattgcaggt gccggatgag 420 gtgaaateet caagegaett getgegette tateaaaaet ggeageetge atgggeteea 480 ggaacacaac gtctgtatgc caactccagt atcggtttgt tcggcgcact ggctgtgaag 540 ccgtctggtt tgagttttga gcaggcgatg caaactcgtg tcttccagcc actcaaactc 600 aaccatacgt ggattaatgt accgcccgca gaagaaaaga attacgcctg gggatatcgc 660 gaaggtaagg cagtgcatgt ttcgcctggg gcgttagatg ctgaagctta tggtgtgaag 720 tegaceattg aagatatgge eegetgggtg caaageaatt taaaaceeet tgatateaat 780 gagaaaacgc ttcaacaagg gatacaactg gcacaatctc gctactggca aaccggcgat 840 atgtatcagg gcctgggctg ggaaatgctg gactggccgg taaatcctga cagcatcatt 900 aacggcagtg acaataaaat tgcactggca gcacgccccg taaaagcgat tacgccccca 960 actcctgcag tacgcgcatc atgggtacat aaaacagggg cgaccggcgg atttggtagc 1020 tatgtcgcgt ttattccaga aaaagagctg ggtatcgtga tgctggcaaa caaaaactat 1080 cccaatccag cgagagtcga cgccgcctgg cagattetta acgctctaca gtaa

Thr Phe Ala Ala Pro Gln Gln Ile Asn Asp Ile Val His Arg Thr Ile 20 25 30

Thr Pro Leu Ile Glu Gln Gln Lys Ile Pro Gly Met Ala Val Ala Val
35 40 45

Ile Tyr Gln Gly Lys Pro Tyr Tyr Phe Thr Trp Gly Tyr Ala Asp Ile
50 55 60

Ala Lys Lys Gln Pro Val Thr Gln Gln Thr Leu Phe Glu Leu Gly Ser
65 70 75 80

Val Ser Lys Thr Phe Thr Gly Val Leu Gly Gly Asp Ala Ile Ala Arg 85 90 95

Gly Glu Ile Lys Leu Ser Asp Pro Thr Thr Lys Tyr Trp Pro Glu Leu 100 105 110

Thr Ala Lys Gln Trp Asn Gly Ile Thr Leu Leu His Leu Ala Thr Tyr 115 120 125

Thr Ala Gly Gly Leu Pro Leu Gln Val Pro Asp Glu Val Lys Ser Ser 130 135 140

Ser Asp Leu Leu Arg Phe Tyr Gln Asn Trp Gln Pro Ala Trp Ala Pro 145 150 155 160

Gly Thr Gln Arg Leu Tyr Ala Asn Ser Ser Ile Gly Leu Phe Gly Ala 165 170 175

Leu Ala Val Lys Pro Ser Gly Leu Ser Phe Glu Gln Ala Met Gln Thr 180 185 190

Arg Val Phe Gln Pro Leu Lys Leu Asn His Thr Trp Ile Asn Val Pro 195 200 205

Pro Ala Glu Glu Lys Asn Tyr Ala Trp Gly Tyr Arg Glu Gly Lys Ala 210 215 220

Val His Val Ser Pro Gly Ala Leu Asp Ala Glu Ala Tyr Gly Val Lys
225 230 235 240

Ser Thr Ile Glu Asp Met Ala Arg Trp Val Gln Ser Asn Leu Lys Pro 245 250 255

Leu Asp Ile Asn Glu Lys Thr Leu Gln Gln Gly Ile Gln Leu Ala Gln 260 265 270

Ser Arg Tyr Trp Gln Thr Gly Asp Met Tyr Gln Gly Leu Gly Trp Glu 275 280 285

Met Leu Asp Trp Pro Val Asn Pro Asp Ser Ile Ile Asn Gly Ser Asp 290 295 300

Asn Lys Ile Ala Leu Ala Ala Arg Pro Val Lys Ala Ile Thr Pro Pro 305 310 315 320

Thr Pro Ala Val Arg Ala Ser Trp Val His Lys Thr Gly Ala Thr Gly 325 330 335

Gly Phe Gly Ser Tyr Val Ala Phe Ile Pro Glu Lys Glu Leu Gly Ile 340 345 350

Val Met Leu Ala Asn Lys Asn Tyr Pro Asn Pro Ala Arg Val Asp Ala 355 360 365

Ala Trp Gln Ile Leu Asn Ala Leu Gln 370 375

<210> 6

<211> 1134

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant ampicillin resistance gene AmpC13A

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<210> 7

<211> 377

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant ampicillin resistance protein AmpC13A

<400> 7

Met Val Lys Thr Thr Leu Cys Ala Leu Leu Ile Thr Ala Ser Cys Ser 1 5 10 15

Thr Phe Ala Ala Pro Gln Gln Ile Asn Asp Ile Val His Arg Thr Ile
20 25 30

Thr Pro Leu Ile Glu Gln Gln Lys Ile Pro Gly Met Ala Val Ala Val 35 40 45

Ile Tyr Gln Gly Lys Pro Tyr Tyr Phe Thr Trp Gly Tyr Ala Asp Ile
50 55 60

Ala Lys Lys Gln Pro Val Thr Gln Gln Thr Leu Phe Glu Leu Gly Ser 65 70 75 80

Val Ser Lys Thr Phe Thr Gly Val Leu Gly Gly Asp Ala Ile Ala Arg 85 90 95

Gly Glu Ile Lys Leu Ser Asp Pro Thr Thr Lys Tyr Trp Pro Glu Leu 100 105 110

Thr Ala Lys Gln Trp Asn Gly Ile Thr Leu Leu His Leu Ala Thr Tyr
115 120 125

Thr Ala Gly Gly Leu Pro Leu Gln Val Pro Asp Glu Val Lys Ser Ser 130 135 140

Ser Asp Leu Leu Arg Phe Tyr Gln Asn Trp Gln Pro Ala Trp Ala Pro 145 150 155 160

Gly Thr Gln Arg Leu Tyr Ala Asn Ser Ser Ile Gly Leu Phe Gly Ala 165 170 175 Leu Ala Val Lys Pro Ser Gly Leu Ser Phe Glu Gln Ala Met Gln Thr 180 185 190

Arg Val Phe Gln Pro Leu Lys Leu Asn His Thr Trp Ile Asn Val Pro 195 200 205

Pro Ala Glu Glu Lys Asn Tyr Ala Trp Gly Tyr Arg Glu Gly Lys Ala 210 215 220

Val His Val Ser Pro Gly Ala Leu Asp Ala Glu Ala Tyr Gly Val Lys 225 230 235 240

Ser Thr Ile Glu Asp Met Ala Arg Trp Val Gln Ser Asn Leu Lys Pro 245 250 255

Leu Asp Ile Asn Glu Lys Thr Leu Gln Gln Gly Ile Gln Leu Ala Gln 260 265 270

Ser Arg Tyr Trp Gln Thr Gly Asp Met Tyr Gln Gly Leu Gly Trp Glu 275 280 285

Met Leu Asp Trp Pro Val Asn Pro Asp Ser Ile Ile Asn Gly Arg Asp 290 295 300

Asn Lys Ile Ala Leu Ala Ala Arg Pro Val Lys Ala Ile Thr Pro Pro 305 310 315 320

Thr Pro Ala Val Arg Ala Ser Trp Val His Lys Thr Gly Ala Thr Gly 325 330 335

Gly Phe Gly Ser Tyr Val Ala Phe Ile Pro Glu Lys Glu Leu Gly Ile 340 345 350

Val Met Leu Ala Asn Lys Asn Tyr Pro Asn Pro Ala Arg Val Asp Ala 355 360 365

Ala Trp Gln Ile Leu Asn Ala Leu Gln 370 375

<210> 8

<211> 1134

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant

ampicillin resistance gene AmpC41A

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<400> 8
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atcccgggta tggcggtggc ggtaatttat cagggtaaac cttattactt tacctggggc 180
tatgcggaca tcgctaaaaa gcagcccgtc acacagcaaa cgttgtttga gttaggttcg 240
gtcagcaaaa catttactgg cgtgcttggt ggcgacgcta ttgctcgagg ggaaatcaag 300
ttaagcgatc ccacaacaaa atactggcct gaacttaccg ctaaacagtg gaatgggatc 360
tcactattac atctcgcaac ctacactgct ggcggcctgc cattgcaggt gccggatgag 420
gtgaaatcct caagcgactt gctgcgcttc tatcaaaact ggcagcctgc atgggctcca 480
ggaacacaac gtctgtatgc caactccagt atcggtttgt tcggcgcact ggctgtgaag 540
ccgtctggtt tgagttttga gcaggcgatg caaactcgtg tcttccagcc actcaaactc 600
aaccatacgt ggattaatgt accgcccgca gaagaaaaga attacgcctg gggatatcgc 660
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gagaaaacgc ttcaacaagg gatacaactg gcacaatctc gctactggca aaccggcgat 840
atgtatcagg gcctgggctg ggaaatgctg gactggccgg taaatcctga cagcatcatt 900
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<210> 9
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<211> 377

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant ampicillin resistance protein AmpC41A

<400> 9

Met Val Lys Thr Thr Leu Cys Ala Leu Leu Ile Thr Ala Ser Cys Ser 1 5 10 15

Thr Phe Ala Ala Pro Gln Gln Ile Asn Asp Ile Val His Arg Thr Ile
20 25 30

Thr Pro Leu Ile Glu Gln Gln Lys Ile Pro Gly Met Ala Val Ala Val
35 40 45

Ile Tyr Gln Gly Lys Pro Tyr Tyr Phe Thr Trp Gly Tyr Ala Asp Ile 50 55.

Ala Lys Lys Gln Pro Val Thr Gln Gln Thr Leu Phe Glu Leu Gly Ser 65 70 75 80

Val Ser Lys Thr Phe Thr Gly Val Leu Gly Gly Asp Ala Ile Ala Arg 85 90 95

Gly Glu Ile Lys Leu Ser Asp Pro Thr Thr Lys Tyr Trp Pro Glu Leu 100 105 110

Thr Ala Lys Gln Trp Asn Gly Ile Ser Leu Leu His Leu Ala Thr Tyr 115 120 125

Thr Ala Gly Gly Leu Pro Leu Gln Val Pro Asp Glu Val Lys Ser Ser 130 135 140

Ser Asp Leu Leu Arg Phe Tyr Gln Asn Trp Gln Pro Ala Trp Ala Pro 145 150 155 160

Gly Thr Gln Arg Leu Tyr Ala Asn Ser Ser Ile Gly Leu Phe Gly Ala 165 170 175

Leu Ala Val Lys Pro Ser Gly Leu Ser Phe Glu Gln Ala Met Gln Thr 180 185 190

Arg Val Phe Gln Pro Leu Lys Leu Asn His Thr Trp Ile Asn Val Pro 195 200 205

Pro Ala Glu Glu Lys Asn Tyr Ala Trp Gly Tyr Arg Glu Gly Lys Ala 210 215 220

Val His Val Ser Pro Gly Ala Leu Asp Ala Glu Ala Tyr Gly Val Lys 225 230 235 240

Ser Thr Ile Glu Asp Met Ala Arg Trp Val Gln Ser Asn Leu Lys Pro 245 250 255

Leu Asp Ile Asn Glu Lys Thr Leu Gln Gln Gly Ile Gln Leu Ala Gln 260 265 270

Ser Arg Tyr Trp Gln Thr Gly Asp Met Tyr Gln Gly Leu Gly Trp Glu 275 280 285

Met Leu Asp Trp Pro Val Asn Pro Asp Ser Ile Ile Asn Gly Arg Asp 290 295 300

Asn Lys Ile Ala Leu Ala Ala Arg Pro Val Lys Ala Ile Thr Pro Pro 305 310 315 320

Thr Pro Ala Val Arg Ala Ser Trp Val His Lys Thr Gly Ala Thr Gly 325 330 335

Gly Phe Gly Ser Tyr Val Ala Phe Ile Pro Glu Lys Glu Leu Gly Ile 340 345 350

Val Met Leu Ala Asn Lys Asn Tyr Pro Asn Pro Ala Arg Val Asp Ala 355 360 365

Ala Trp Gln Ile Leu Asn Ala Leu Gln 370 375

<210> 10

<211> 1134

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant ampicillin resistance gene AmpC21B

<400> 10 atggtcaaaa cgacgctctg cgccttatta attaccgcct cttgctccac atttgctgcc 60 cctcaacaaa tcaacgatat tgtgcatcgc acaattaccc cgcttataga gcaacaaaag 120 atcccgggta tggcggtggc ggtaatttat cagggtaaac cttattactt tacctggggc 180 tatgcggaca tcgccaaaaa gcagcccgtc acacagcaaa cgttgtttga gttaggttcg 240 gtcagcaaaa catttactgg cgtgcttggt ggcgacgcta ttgctcgagg ggaaatcaag 300 ttaagcgatc ccacaacaaa atactggcct gaacttaccg ctaaacagtg gaatgggatc 360 acactattac atctcgcaac ctacactgct ggcggcctgc cattgcaggt gccggatgag 420 gtgaaateet caagegaett getgegette tateaaaaet ggeageetge atgggeteea 480 ggaacacaac gtctgtatgc caactccagt atcggtttgt tcggcgcact ggctgtgaag 540 ccgtctggtt tgagttttga gcaggcgatg caaactcgtg tcttccggcc actcaaactc 600 aaccatacgt ggattaatgt accgcccgca gaagaaaaga attacgcctg gggatatcgc 660 gaaggtaagg cagtgcatgt ttcgcctggg gcgttagatg ccgaagctta tggtgtgaag 720 tegaceattg aagatatgge eegetgggtg caaagcaatt taaaacecet tgatateaat 780 gagaaaacgc ttcaacaagg gatacaactg gcacaatctc gctactggca aaccggcgat 840 atgtatcagg gcctgggctg ggaaatgcgg gactggccgg taagtcctga cagcatcatt 900 aacggcagtg acaataaaat tgcactggca gcacgccccg taaaagcgat tacgccccca 960 actcctgcag tacgcgcatc atgggtacat aaaacagggg cgaccggcgg atttggtagc 1020 tatgtcgcgt ttattccaga aaaagagctg ggtatcgtga tgctggcaaa caaaaactat 1080 cccaatccag cgagagtcga cgccgcctgg cagattctta acgctctaca gtaa

<210> 11

<211> 377

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mutant ampicillin resistance protein AmpC21B

Thr Phe Ala Ala Pro Gln Gln Ile Asn Asp Ile Val His Arg Thr Ile
20 25 30

Thr Pro Leu Ile Glu Gln Gln Lys Ile Pro Gly Met Ala Val Ala Val
35 40 45

Ile Tyr Gln Gly Lys Pro Tyr Tyr Phe Thr Trp Gly Tyr Ala Asp Ile 50 55 60

Ala Lys Lys Gln Pro Val Thr Gln Gln Thr Leu Phe Glu Leu Gly Ser 65 70 75 80

Val Ser Lys Thr Phe Thr Gly Val Leu Gly Gly Asp Ala Ile Ala Arg 85 90 95

Gly Glu Ile Lys Leu Ser Asp Pro Thr Thr Lys Tyr Trp Pro Glu Leu 100 105 110

Thr Ala Lys Gln Trp Asn Gly Ile Thr Leu Leu His Leu Ala Thr Tyr 115 120 125

Thr Ala Gly Gly Leu Pro Leu Gln Val Pro Asp Glu Val Lys Ser Ser 130 135 140

Ser Asp Leu Leu Arg Phe Tyr Gln Asn Trp Gln Pro Ala Trp Ala Pro 145 150 155 160

Gly Thr Gln Arg Leu Tyr Ala Asn Ser Ser Ile Gly Leu Phe Gly Ala 165 170 175

Leu Ala Val Lys Pro Ser Gly Leu Ser Phe Glu Gln Ala Met Gln Thr 180 185 190

Arg Val Phe Arg Pro Leu Lys Leu Asn His Thr Trp Ile Asn Val Pro 195 200 205

Pro Ala Glu Glu Lys Asn Tyr Ala Trp Gly Tyr Arg Glu Gly Lys Ala 210 215 220

Val His Val Ser Pro Gly Ala Leu Asp Ala Glu Ala Tyr Gly Val Lys 225 230 235 240

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